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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|--------------------------|---------------------|------------------|
| 09/992,174 | 11/14/2001 | Mario Anthony Moscarello | 2132.024 | 6896 |

21917 7590 11/13/2007
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| EXAMINER |
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COUNTS, GARY W

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| ART UNIT | PAPER NUMBER |
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1641

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| MAIL DATE | DELIVERY MODE |
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11/13/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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|------------------------------|--------------------------------------|---|--|
| Office Action Summary | Application No. 09/992,174 | Applicant(s) MOSCARIELLO ET AL. | |
| | Examiner Gary W. Counts | Art Unit 1641 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the claims

The amendment filed October 10, 2007 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 22-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 the recitation "providing an enzyme-linked immunosorbent assay (ELISA) which has immobilized thereon myelin basic protein" is vague and indefinite. It is unclear how the assay has myelin basic protein immobilized on it. Does applicant intend that the assay comprising some type of solid phase having myelin basic protein immobilized on the solid phase or does applicant intend something else. The claim as written is confusing as to what applicant is trying to encompass.

Claim 22 step (e) is vague and indefinite because it is unclear what applicant intends by the recitation "comparing said level of said at least one autoantibody with statistically significant levels thereof known to be indicative of diseased versus normal individuals". Does applicant intend that the level is compared to a level of diseased patients which are considered to have values that are statistically significant levels? Does applicant intend that the level is compared to a healthy control patient and levels above specific standard deviations are considered statistically significant or does

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applicant intend something else? The specification on page 25 discloses comparison to healthy controls. The specification on page 35 discloses two standard deviations difference between MS patients and controls? For purposes of examination the Examiner has interpreted the recitation to intend the comparison to a control and the level compared to the control is determined to be statistically significant.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Voumvourakis et al (Detection of anti-MBP in the serum of patients with multiple sclerosis, Greek Microbiology Organization Newsletter (1992) 37, 666-672) in view of Pesce et al (Cationic antigens Problems associated with measurement by ELISA, Journal of Immunological methods, 87 (1986) 21-27).

Voumvourakis et al disclose a method wherein a serum sample is obtained from an MS patient. Voumvourakis et al discloses that the sample is subjected to an ELISA assay wherein an immobilized myelin basic protein (MBP) (cationic protein) is used to capture and determine levels of anti-MBP IgG and anti-MBP IgM. Voumvourakis et al discloses that the determined levels are compared to healthy controls (p. 668) and statistically significant levels are determined for the IgG antibodies (p. 668).

Voumvourakis et al differ from the instant invention in failing to teach the utilization of heparin to reduce non-specific charge interactions with MBP.

Pesce et al disclose the use of heparin to reduce non-specific charge interactions of cationic proteins that plague the sensitivities of ELISAs. Pesce et al disclose the addition of heparin with the sample prior to carrying out the assay (p. 23). Pesce et al disclose that non-specific reactivity of the cationic protein could almost completely be eliminated by carrying out the antibody-antigen incubation in the presence of heparin (p. 23) and further discloses that the use of heparin allows for the

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enhancement of antigen-antibody reactions because of neutralization of the positive charges on the antigen (p. 27).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the use of heparin as taught by Pesce et al into the method of Voumvourakis et al because Pesce et al shows that non-specific reactivity of the cationic protein (MBP is cationic) can almost completely be eliminated by carrying out the antibody-antigen incubation in the presence of heparin and further discloses that the use of heparin allows for the enhancement of antigen-antibody reactions because of neutralization of the positive charges on the antigen. Therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating heparin as taught by Pesce et al into the method of Voumvourakis et al.

7. Claims 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Voumvourakis et al and Pesce et al in view of Landry (5,736,343) or Bishop et al., (Clinical Chemistry 2nd edition, 1992, pages 70-71).

See above for the teachings of Voumvourakis et al and Pesce et al.

Voumvourakis et al and Pesce et al differ from the instant invention in failing to teach first and second samples obtained at different times.

Landry discloses that it is known in the art that for monitoring the course of a disease in a subject that first and second samples are taken at different time intervals and comparing the amounts determined in order to indicate the course of the disease (col 15).

Bishop et al discloses that it is known in the art for monitoring that a test result is compared with values previously obtained from the same patient (col 71).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate comparison steps to previously obtained values because both Landry and Bishop show that it is known in the art to compare values to previous obtained values in order to provide the monitoring of a disease. Thus, one of ordinary skill in the art would have a reasonable expectation of success comparing the values to previously obtained values to monitor the progression of a disease.

Response to Arguments

8. Applicant's arguments filed October 10, 2007 have been fully considered but they are not persuasive.

Applicant argues that while it is possible to combine the teachings of Voumvourakis et al and Pesce et al , the Examiner is respectfully reminded that the fact that references can be combined or modified does not render the resultant combination obvious unless the prior art suggest the desirability of the combination. This is not found persuasive because KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, --USPQ2s--, slip op. at 20 (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396)(available at <http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf>).

Applicant further argues that while Pesce et al indicate that other polycationic molecules might share what he terms "unique" properties, it is respectfully submitted

that a skilled artisan, absent the instant inventor's own disclosure, would not look to promulgating an obviousness rejection by utilizing the combination of Voumvourakis et al and Pesce et al, since there is not teaching or suggestion that the instant inventor's unique combination would fall within this disclosure. This is not found persuasive because of KSR stated above. Applicant further argues that there is no intrinsic or inherent suggestion in the references other than the impermissible use of hindsight. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant rejection Voumvourakis et al teaches using a cationic protein in an ELISA assay and Pesce et al specifically teaches the advantages of using heparin in ELISA assays employing cationic proteins and teaches that the addition of heparin to such assays provides for the non-specific reactivity of the cationic protein (MBP is cationic) to be almost completely eliminated by carrying out the antibody-antigen incubation in the presence of heparin and further discloses that the use of heparin allows for the enhancement of antigen-antibody reactions because of neutralization of the positive charges on the antigen. Thus, one of ordinary skill in the art would want to enhance the antigen-antibody reaction of the Voumvourakis assay.

Applicant argues that obviousness to try is not a valid basis for an obviousness holding. This is not found persuasive because contrary to applicant's arguments, the combination of Voumvourakis et al and Pesce et al is not a mere obvious to try. Although, Pesce et al exemplifies BSA his entire teaching encompasses all cationic proteins which Voumvourakis et al is using and the teachings of Pesce et al well encompasses the MBP taught by Voumvourakis et al and for the reasons stated above the combination of Voumvourakis et al in view of Pesce et al is considered appropriate and reads on the instantly recited claims.

Conclusion

9. No claims are allowed.
10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed; and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Gary Counts
Examiner
Art unit 16413
November 2, 2007



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